

Race to Fill Void in Menopause-Drug Market

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In the eight weeks since the federal government announced that it had halted a study of a popular hormone therapy used by postmenopausal women, doctors say they have been deluged by an ever-growing tide of promotional material for anything and everything that could substitute for Prempro, the drug used in the study.

The alternatives run the gamut: prescription drugs that consist of slightly different hormone formulations, nutritional supplements made of herbs and vitamins, soy products said to be natural sources of estrogen, and even what might be termed menopause accessories, such as one company's "cooling comfort towelettes" to wipe the sweat from hot flashes.

But many doctors and scientists say they are alarmed by the profusion of Prempro substitutes. The trouble, they say, is that these drugs and supplements have been studied less than Prempro has. Their benefits and risks are simply unknown.

That is especially true for nutritional supplements. Their advertising receives far less government scrutiny than claims for prescription drugs, which the Food and Drug Administration regulates closely.

They are also sold without a doctor's guidance. "Everything you've ever heard of is being marketed," said Dr. Wulf Utian, the executive director of the North American Menopause Society, "and it's being marketed to a confused and vulnerable population."

Prempro, a combination of estrogens and progestin made by Wyeth, has long dominated the menopause market. Until this summer it was used by six million American women, many of whom assumed they would be taking it for a lifetime to protect against some effects of aging, like brittle bones.

But when the federal study, the Women's Health Initiative, found that Prempro carried slight risks (of heart attack, stroke and breast cancer) that outweighed its benefits (a slightly lower risk of colon cancer and hip fracture), the part of the study in which women were taking Prempro was ended. A study in which women take estrogen alone continues. A Wyeth spokesman, Doug Petkus, said sales of Prempro had declined 25 to 30 percent.

Many companies appear to have rushed into the opening. "The Women's Health Initiative Study wasn't out of my fingers before the mailings started coming in," said Dr. Nanette Santoro, a professor of obstetrics and gynecology at Albert Einstein College of Medicine and the Montefiore Medical Center in the Bronx. "It's what you expect in a capitalist economy. You have people with products to sell."

Prempro, like other estrogen replacements, is clearly effective against some symptoms of menopause, including hot flashes and vaginal dryness. Dr. Isaac Schiff, chief of obstetrics and gynecology at the Massachusetts General Hospital, said the government's findings touched off "a mild to severe panic" and left some women desperate for alternatives.

"Now we are seeing the fallout," Dr. Schiff said. "They are saying, 'The hot flashes are killing me,' or 'I don't feel well.'" Some of his patients tell him they have lost energy or a sense of well-being.

"They are trying to go back on estrogen," Dr. Schiff said. But, he added, "They do not want to go on Prempro."

While the level of marketing for alternative drugs and supplements is impossible to quantify in the short time since the findings about Prempro were reported, Dr. Schiff and others say they have been bombarded with fliers, e-mail promotions and visits from drug salespeople. A similar barrage is going out to patients, in the form of advertisements in newspapers and magazines, in the mail and on the Web.

The American College of Obstetricians and Gynecologists has warned its members that it is not necessarily safe to switch women from Prempro to other prescription hormones, adding, "Caution is warranted for different preparations, and their safety should not be assumed in the absence of conclusive data."

But prescription hormones are only part of the picture. Doctors say they are particularly concerned about the promotion of nutritional supplements.

The college of obstetricians, for example, cautions, "The number and sophistication of most studies on alternative therapies, including botanicals, do not meet the current standards of evidence-based recommendations." It adds that " 'natural' does not mean safe or effective," and that "potentially dangerous or lethal drug-herb interactions can occur."

The National Institutes of Health's National Center for Complementary and Alternative Medicine also cautions women on its Web site, <http://nccam.nih.gov/health/alerts/menopause/>, about the claims being made for vitamins, herbs and products like soy that contain plant estrogens.

"At this time, there is not enough scientific evidence to determine whether these therapies are beneficial," the Web site says. "In addition, we do not have sufficient information to show whether these therapies are as safe or safer than conventional drugs being used for menopausal symptoms, osteoporosis or heart disease."

Makers of the supplements assert that they are safe and effective. Gayle Engles, education director for the Botanical Council, a nonprofit group that disseminates

information on herbal medicines, says that many of the products have been in use for hundreds of years and that some have been tested in scientific studies.

Still, Dr. Utian, of the menopause society, said that too many companies were sending a message he paraphrased this way: "The Women's Health Initiative has shown the other stuff is garbage, but we have the answer."

He cited an e-mail promotion with the headline: "Women Search for a Safe Alternative to Hormonal Replacement Therapy. Scientific Research Already Has the Answer." The company, SuperNutrition, says its vitamin and herb combination called Menopause Multiple Blend prevents hot flashes, strengthens bone, protects against heart disease, prevents memory problems and, best of all, is "safe and natural."

Makers of other products also advertise benefits that groups like the National Institutes of Health say are not demonstrated.

Whole World Botanicals advertises a Peruvian herb, maca, asserting that it can relieve symptoms of menopause and even help with "premenstrual syndrome" in younger women. The herb, its maker claims, "contains no plant hormones, unlike soy/genistein and black cohosh."

Zoe Foods says its soy cereals and bars "have helped thousands of women overcome their menopausal symptoms." Another company, SoyToy, claims its soy juicer makes milk from soybeans in 25 minutes. Soy, it says, alleviates symptoms of menopause, increases bone mass and decreases the risk of heart disease.

GlaxoSmithKline, the large drug company best known for its prescription drugs, touts the benefits of another diet supplement, black cohosh, which it markets as Remifemin. The package states that Remifemin is "drug free" and "estrogen free" and that it is good for hot flashes, night sweats, mood swings, irritability and related occasional sleeplessness. A footnote informs consumers, "These statements have not been evaluated by the Food and Drug Administration."

Other companies offer custom blends of actual estrogens and progestins. Individual states, rather than the F.D.A., normally regulate these products as they regulate pharmacies.

Dr. Schiff, at Massachusetts General, pointed to a flier from one such company, the Women's International Pharmacy, advertising "bio-identical hormones" and "customized prescriptions" and claiming that its product is safer than hormones sold by drug companies. "They have no evidence for that," Dr. Schiff said.

Makers of prescription estrogens and progestins take a different tack, he said. Because those drugs are regulated by the F.D.A., they may not make unproven claims.

"I have been bombarded with very subtle ads," Dr. Schiff said. "They can't say their product is safer because they don't have the evidence." Instead, he said, they try an indirect approach: "We make product ABC and we don't make the product that was involved in the Women's Health Initiative.' It is like having a bad relative and making sure you don't sit next to them. They are pushing themselves away from the table."

Dr. Marcia L. Stefanick of Stanford University, the principal investigator for the Women's Health Initiative, said some doctors were too quick to say that the risks of Prempro were specific to Prempro but not to other formulations of estrogens and progestins - or that estrogens from plants were safe because they are "natural."

The estrogens in Prempro, Dr. Stefanick said, "are as natural to the horse as the phytoestrogens are to the South American yam." As for soy, she asked, "If it is natural to a soy plant, does that make it natural to humans?"

<http://www.nytimes.com/2002/09/01/health/womenshealth/01MENO.html?ex=1031906512&ei=1&en=5147467c1a165041>